Bipolar disorder with late onset: an organic variety of mood disorder?

Transtorno bipolar de início tardio: uma variedade orgânica do transtorno de humor?

Osvaldo P Almeida

Abstract

Bipolar disorder (BD) is commonly associated with late adolescence or early adulthood, although a substantial proportion of patients develops the condition in later life. The results of early clinical investigations suggested that cases of BD with onset in later life were more often associated with ‘organic causes’, and could potentially justify the distinction between early and late onset BD. This paper reviews currently available evidence in support of the organic hypothesis for late onset BD. It concludes that the split of BD according to age at onset is artificial, and lacks clinical significance and epidemiological support.

Keywords: Bipolar disorder/etiology; Mood disorders/complications; Aged

Resumo

Transtorno bipolar (TB) é comumente associado à fase final da adolescência ou idade adulta jovem, embora em uma proporção substancial dos pacientes a doença comece em fases mais tardias da vida. Os resultados de várias investigações clínicas sugerem que casos de transtorno bipolar com início tardio têm, mais freqüentemente, uma “causa orgânica” e que isso justificaria a subdivisão do transtorno bipolar entre “início precoce” e “início tardio”. Este artigo revê a literatura sobre a hipótese orgânica do transtorno bipolar de início tardio e conclui que essa subdivisão é artificial e carece de suporte clínico e epidemiológico.

Descritores: Transtorno bipolar/etiologia; Transtorno do humor/complicação; Idoso

Introduction

Bipolar disorder (BD) is a condition commonly associated with late adolescence and early adulthood. The onset of symptoms is usually placed between the ages of 18 and 22 years, although a substantial proportion of patients develop the condition later in life. Almeida and Fenner, for example, found that 492/6182 patients with BD had illness onset at or after the age of 65 years (8% of the total sample), confirming that mania may arise for the first-ever time amongst older adults. Broadhead and Jacoby confirmed that silent cerebral infarcts are observed more frequently amongst subjects with late onset BD (13/20) than older adults (36 subjects with late onset BD). This paper reviews currently available evidence in support of the organic hypothesis for BD with late onset. It concludes that the split of BD according to age at onset is artificial, and lacks clinical significance and epidemiological support.

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Frontotemporal dementia (FTD) is another neurodegenerative condition typically associated with mania-like symptoms and behaviours. Cross-sectional studies have shown that disinhibition and euphoria are more frequent amongst patients with FTD (68% and 36% respectively) than AD (23% and 7%)[14] and that irritability and agitation are also common[15,16]. In fact, symptoms like psychomotor agitation and aggressive behaviour have been associated with frontotemporal pathology not only in patients with FTD but also AD.[17] For example, Forlenza et al[18] found that agitation was significantly correlated with the number of neurofibrillary tangles in the left orbitofrontal cortex of patients with AD.

The diagnosis of a dementia syndrome has also been associated with increased risk of manic episodes at follow-up. Nilsson et al[19] used the Danish Psychiatric Central Register and the National Hospital Register to investigate the hazard of 28,594 subjects with dementia, 108,152 with osteoarthritis and 90,948 with diabetes mellitus developing an affective disorder during a follow-up period of up to 21 years. They found that older adults with dementia were 9.9 (95%CI=4.2-23.2) times more likely to develop mania within the initial 6 months of follow-up, and 21.1 (95%CI=4.2-105.3) and 6.9 (95%CI=4.6-10.5) times more likely than controls to receive the diagnosis of mania after 6-12 months and 12 or more months respectively. They concluded that once the diagnosis of dementia is established, patients remain at increased risk of experiencing an affective episode (including depression and mania) for the rest of their lives.

Vascular dementia, Huntington’s disease, normal pressure hydrocephalus and prion diseases have also been associated with mania.[19,20] However, there is no compelling evidence that the symptoms associated with these conditions would be mistakenly attributed to a primary manic episode.

3. Other neurological disorders

Brain injury, epilepsy, brain tumours, encephalitis and various forms of cerebral infection have been associated with manic symptoms.[21] The effects of traumatic brain lesions on mood have been reviewed by Starkstein and Robinson.[22] They highlighted that approximately 10% of closed head injury survivors meet criteria for the diagnosis of mania during the subsequent 12 months, and argued that manic symptoms are more likely to arise amongst patients with orbitofrontal, basotemporal and diencephalic lesions. Of interest, a recently published Case Register study from Denmark found that their 10,242 patients with BD were 55% (95%CI=36%-77%) more likely than the 102,420 matched controls to have had a medical contact for head injury during the 5 years prior to diagnosis,[22] reinforcing the view that brain injury may be associated with the onset of manic symptoms.

Brain tumours can also be associated with an array of neuropsychiatric symptoms, including mania. Filley and DeMasters[23] argued, in their review of the subject, that frontal lobe neoplasms are more frequently associated with apathy, whereas symptoms of mania seem more likely to arise amongst patients with basotemporal tumours. However, information on this topic remains sparse and limited to a few case-reports and small case-series.

Epilepsy is another neurological condition that has been associated with mania. Almeida[24] reported that 1/29 consecutive older outpatients with epilepsy met diagnostic criteria for mania (mean age = 66.0 years). Case-reports have also suggested that complex partial seizures may give rise to manic symptoms amongst older adults[25] but, again, there is no substantial evidence to support such a hypothesis.

Various infections of the central nervous system have been associated with symptoms of mania as well. For example, Forlenza et al[26] reported that 1/38 patients aged 18-60 years with neurocysticercosis consecutively assessed at an outpatient service of neurology met criteria for the diagnosis of mania according to the Research Diagnostic Criteria (RDC). The frequency of mania was much higher in the group of patients investigated by Tavares Jr[27] – he identified 13 cases of mania in his retrospective study of 25 patients with neurocysticercosis, although his sample was specifically selected to include patients with neurobehavioural disorders. General paresis, which is now an extremely rare form of neurosyphilis, is typically associated with grandiose or expansive mood in adults aged 30-50 years.[28] Other infections of the central nervous system, such as herpes simplex, HIV, toxoplasmosis and criptococcal meningitis, have also been reported in association with symptoms of mania,[29] but these are rather uncommon in later life.

Other conditions associated with mania in later life

The list of conditions that might lead to the development of manic symptoms in later life is long,[3] but probably unreliable. Publication bias is likely to have contributed to the reporting of spurious secondary causes of mania, such vitamin B12 deficiency. Vitamin B12 deficiency is common amongst older adults aged 70 years or over (approximately 10% in community-representative samples),[30] and it seems likely that its association with mania described in case-reports has arisen by chance. Other less common conditions, such as hyperthyroidism and Cushing’s syndrome have also been associated with manic symptoms. Kelly[31] reported that 3% of a series of 209 patients with Cushing’s syndrome presented with mania or hypomania, whereas Oomen et al[32] found that approximately 1/3 of patients admitted to three psychiatric hospitals with the diagnosis of mania showed laboratory signs of hyperthyroidism. Case-reports have also suggested that hyperthyroidism may lead to clinical presentations consistent with the diagnosis of BD amongst the elderly,[33] but substantial data in support of such an association is still not available.

Several medications have been reported as potential causes of mania amongst young and older adults. The use of corticosteroids, particularly when used in relatively high dosages, is associated with the development of hypomanic or manic symptoms in approximately 1/4 patients.[34] However, it seems unlikely that mania associated with corticosteroid use would be wrongly attributed to BD, as there is a tight temporal relationship between the introduction of the medication and development of symptoms (3-5 days). The use of stimulant agents, such as amphetamines and cocaine, are also widely accepted as potential causes of mania, but information on this topic is understandably limited to case-reports and small case-series, mostly of young rather than older adults. For the elderly population, a potentially important cause of secondary mania is the use of antidepressants. The consumption of antidepressants, particularly SSRIs, has increased dramatically over the past decade[35] and, if they do induce manic symptoms, one would expect to see a significant increase in the number of cases diagnosed with BD. This does not seem to have been the case. In a recent review of this topic, Chun and Dunner[36] observed that the proportion of people who developed mania in randomised and open-label trials does not exceed the expected rate of misdiagnosis of BD as unipolar depression. They concluded that patients who experience mania or hypomania in association with antidepressant treatment are likely to have true BD rather than antidepressant induced mania.
Symptoms typically arise amongst people in their 20s, affects approximately 0.4% of the population over a 19-year period. The ‘organic hypothesis’ of late onset BD implies that a large proportion of adults who experience their first ever episode of mania or hypomania in later life have, in fact, a ‘secondary’ form of mood disorder. If such a hypothesis is true, one would expect to see an increase in the number of older adults with BD with increasing age, as the frequency of neurodegenerative conditions, cerebrovascular disease, cancer and use of medications rises sharply for people in their 70s and 80s. We have recently evaluated the age at onset of illness in this population, as had been previously suggested by Broadhead and Jacoby5 (Figure). Of Western Australia according to their age at onset (modified from Almeida and Fenner, 2002).

Figure 1 - Frequency distribution of cases of bipolar disorder in Western Australia according to their age at onset (modified from Almeida and Fenner, 2002).

Comments

The ‘organic hypothesis’ of late onset BD implies that a large proportion of adults who experience their first ever episode of mania or hypomania in later life have, in fact, a ‘secondary’ form of mood disorder. If such a hypothesis is true, one would expect to see an increase in the number of older adults with BD with increasing age, as the frequency of neurodegenerative conditions, cerebrovascular disease, cancer and use of medications rises sharply for people in their 70s and 80s. We have recently evaluated the age at onset of the entire population of patients with BD in contact with the Western Australian health services between 1980 and 1998.4 We found no evidence for a bimodal distribution of the age at onset of illness in this population, as had been previously suggested by Broadhead and Jacoby5 (Figure). Of course, this finding could be potentially explained by the fact that these patients might have been correctly diagnosed as suffering from an organic mental disorder rather than BD. However, the frequency of patients who received the diagnosis of organic mental disorder during the study-period was very low (0.8%) and could not adequately explain the findings of the study.

Bipolar disorder is a relatively uncommon mental illness that affects approximately 0.4% of the population over a 19-year period.4 Symptoms typically arise amongst people in their 20s, but the onset of the illness is certainly not limited to young adulthood. Whilst an array of medical conditions and drugs are thought to increase the risk of mania, their presence cannot adequately explain the relatively large proportion of cases of BD with onset in later life. It is good clinical practice to investigate the presence of potentially modifiable factors amongst patients presenting for the first-ever time with an episode of mania, although there is no reason to limit such an approach to older adults, as secondary mania can potentially affect any age group. It seems, therefore, unjustifiable to use the potential (and infrequent) ‘organic basis’ of some cases of BD to separate patients into an early and late onset group. Such a division is artificial and lacks clinical significance and epidemiological support.

References


Correspondence
Osvaldo P Almeida
School of Psychiatry and Clinical Neurosciences, University of Western Australia
Mail Point 573 (Ainslie House, Royal Perth Hospital), 35 Stirling Highway, Crawley, Perth WA 6009, Australia
Email: osvalm@cyllene.uwa.edu.au